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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/723,256	11/27/2000	R. Terry Dunlay	97,022-B1	5678

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EXAMINER	
SMITH, CAROLYN L	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 09/23/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/723,256	DUNLAY ET AL.	
	Examin r	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30,44,54 and 61-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30, 44, 54, 61-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendments and remarks in Paper No. 15, filed 7/17/03, are acknowledged. Amended claims 30, 44, 54, and 64 and cancelled claims 45-50, 55, and 57-60 are acknowledged.

Applicant's arguments, filed 7/17/03, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

In the Response on pages 2 and 3, claims 1-29 and 31-43 are listed having a "previously withdrawn" status. This is incorrect. The correct status of these claims is "previously canceled."

The new title, filed 7/17/03, is accepted by the Examiner.

Claims 30, 44, 54, and 61-65 are herein under examination.

Specification

The specification contains markings that are improper. Replacement paragraphs are required which do not contain these markings. Such marks are present on pages 6, 7, 9, 21, 27, 28, 31, 34, 53, 54, 59, 62, 68, 69, 70, 76, 78, and 79.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the

subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. (e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicants argue that not all of the claim limitations have been addressed, particularly involving cell membrane and cytoplasm. New prior art is listed below.

Claims 30, 44, 54, and 61-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cabib et al. (P/N 5,784,162) in view of *In re Venner* (262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958)).

Cabib et al. describe bio-imaging methods involving measurements and analysis software that detect spatial organization, such as distribution, and quantify cellular constituents, structures, organelles and administered components such as tagged fluorescent probes and drugs (test stimulus) using light transmission, reflection, scattering, and fluorescence emission strategies (col. 1, lines 13-25 and col. 2, lines 3-4). Cabib et al. describe using the method for cell and tissue classification, in drug development research as well as mapping cytoplasm organelles and constituents and the cell membrane (col. 10, line 62 to col. 11, line 12 and col. 38, line 17 to col. 39, line 9). Cabib et al. describe algorithms to interpret spectral information of chemical

elements (concentration mapping) and/or morphological interpretation using image shapes (col. 61, lines 33-45). Cabib et al. describe using the cell, tissue or organism samples to monitor life processes in the sample as a function of time (col. 11, lines 30-34). Cabib et al. describe scanning of multiple cells in an array of locations using an image spectrometer as seen in Figure 1 (col. 16, lines 36-67). Cabib et al. describe measuring spatial separation between at least two fluorophores where one is administered to the sample (col. 11, lines 13-18). Cabib et al. describe using spectral imaging to detect proteins and nucleic acid sequences after being labeled with fluorescent probes, mapping, and sorting out several fluorophores in one measurement (col. 1, lines 41 and 56-66) as stated in claims 30 and 61. Cabib et al. describe measuring fluorescent from various constituents including cytoplasmic proteins in the sample (col. 10, lines 57-61). Cabib et al. describe using a fluorescently labeled antibody (col. 8, lines 52-55) as stated in claim 62. Cabib et al. describe the spectral imaging enables detection at any location in the image (col. 1, lines 66-67). Cabib et al. describe spectral dispersion methods with filters which insert filters in the optical path (col. 2, line 66 to col. 3, line 13) which represents masking. Cabib et al. describe work done on imaging one or a few points of a sample (col. 3, lines 39-44). Cabib et al. describe using the system to detect differences between chemical constituents whose spatial distribution and organization is of interest along with using a filtering method such as dark field, phase contrast, and polarized light microscopy (col. 5, lines 23-45 and col. 36, lines 16-50) which represents masking. Cabib et al. describe the bio-imaging system can measure spectral differences in different parts of the cell to provide insight in to the functions of the organelles in a living cell (col. 34, lines 39-42). Cabib et al. describe identifying multiple fluorophores and using time resolved spectral imaging (col. 5, lines 46-60 and col. 8, lines 56-61). Cabib et al.

describe measuring emission spectra for identifying and mapping biological components, such as proteins, within cancerous and healthy cells and tissues using various fluorescing tags (col. 6, lines 27-53). Cabib et al. describe analyzing similarity mapping to determine differences between a sample and one or more references with color changes corresponding to the intensity of the differences (col. 9, lines 13-22 and 33-43). Cabib et al. describe a ratio of integrated intensity of spectral values or signals (col. 9, lines 28-32 and col. 10, lines 39-52). Cabib et al. describe the image of the sample is stationary on the plane of the detector array (col. 7, lines 23-36) which means the sample itself is stationary or fixed. Cabib et al. describe a signal is a particular combination of light intensity emitted by the pixel at different wavelengths and the presence and level of the signals is detected (col. 7, lines 30-36 and col. 8, lines 36-41). Cabib et al. describe recording signals as a function of time (col. 7, lines 40-43) which is reasonably interpreted to mean that measurements of light intensities are taking at multiple time points, including a first and second time point. Cabib et al. describe identifying nucleic acid probes for disease genes by marking probes with examined chromosomal regions as well as cell, tissue and gene identification and mapping (col. 5, line 61 to col. 6, line 5; col. 8, lines 47-51; and col. 10, line 62 to col. 11, line 8) which represents nucleic acid identification in cells as stated in claim 44. Cabib et al. describe displaying the bio-imaging map of the spectral cube of data (col. 7, lines 44-48). Cabib et al. describe finding which elements tag certain features in the sample (col. 9, lines 59-61). Cabib et al. describe analyzing wavelength signals from a first spectral cube of data to a second cube of data to obtain a resulting third spectral cube of data, including looking at time change follow-ups (col. 9, line 65 to col. 10, line 9). Cabib et al. describe a calibration procedure is used where the viewing is sample is divided (col. 10, lines 23-27). Cabib et al.

describe the system can be used by surgeons before, during, or after surgery (col. 58, lines 22-33) which represents the use of live tissue and cells as stated in claim 65. Cabib et al. describe classification analysis and morphological analysis involved in the spectral analysis (col. 12, lines 15-18 and 56-65). Cabib et al. also describe black and white intensity images in Figure 30 (a-c) (col. 16, lines 5-9). Cabib et al. describe chlorophyll fluorescent intensities in the cell as opposed to the cell membrane allowing the visualization of fluorescence emitted from specific subcellular regions in the cell (col. 34, line 25 to col. 35, line 13). Cabib et al. do not mention a machine readable storage medium, but do computer software and hardware and mention other existing devices may attach to the device in their invention (col. 61, lines 46-53).

Although Cabib et al. describe the above-mentioned method in a computer hardware and software program, they do not describe having this program on a machine readable storage medium using computer-executable instructions. *In re Venner* 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) states that it is obvious to computerize a manual activity. The court held that broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over prior art as stated in MPEP § 2144.04, Part III.

Cabib et al. state the widely recognized need for bio-imaging methods which provide advanced means to detect spatial organization, quantify, and display cellular components, probes, and drugs using various light and fluorescent technologies (col. 6, lines 54-62). Cabib et al. state the widely recognized need to increase objectivity and reliability of tests and to automate the prescreening stage (col. 59, lines 8-14). Cabib et al. state that other existing devices may attach to the device in their invention (col. 61, lines 46-53). A person of ordinary skill in the art

would have been motivated to further develop ways of analyzing resulting signals and images from diagnostic detection systems as stated by Cabib et al., by including these steps on a computer readable medium in order to impart understanding of the images regarding chemical, physiologic, and pathologic indications to a diagnostician, researcher, or surgeon as stated by Cabib et al. (col. 4, lines 1-4). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to place the analysis software on a machine readable storage medium for a manual activity (as discussed by In re Venner), because this would allow for interpretation of spectral information with present and future algorithms as well as allowing for comparisons to be made between data to enable fast and very versatile work, as stated by Cabib et al.(col. 60, last paragraph and col. 61, fourth paragraph).

Thus, Cabib et al., in view of *In re Venner*, motivate the instant invention.

The effective filing date for claims including the phrase "cell membrane" is the actual filing date of this application (11/27/00) as no mention of "cell membrane" appears in the priority documents.

Claims 30, 44, 54, and 61-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. (P/N 6,388,788) in view of *In re Venner*.

Harris et al. describe a method and apparatus for screening pharmaceutical compounds in fluorescent assays, including live cell assays (abstract). Harris et al. describe analyzing images to determine the amount of a first fluorescently labeled species localized compared to a second fluorescently labeled species (col. 25, lines 49-54) which is a form of distribution detection. Harris et al. describe the method involving real time data-processing at video rates (abstract). Harris et al. disclose screening proteins (col. 1, lines 44-56). Harris et al. describe using

fluorescent dyes applied to cells on the bottom of the wells of a multi-well plate and scanning the sample which remains at a fixed position (col. 1, lines 60-67; col. 6, lines 45-57; and col. 7, lines 38-40 and 54-61). Harris et al. describe using a multi-parameter fluorescence imaging on single cells and cell populations (col. 2, lines 53-56). Harris et al. describe the ability to determine the locations of the multiple fluorophores with sub-cellular resolution (col. 2, lines 60-61). Harris et al. describe the target of interest may be in a cell, subcellular organelle, or on the cell membrane (col. 7, lines 7-10). Harris et al. describe translocation assays with two or more fluorescently-labeled species, such as proteins, from one well-defined region of the cell to another (col. 26, line 63 to col. 27, line 7). Harris et al. describe comparing first and second species co-localized and various ratios among them (col. 27, lines 8-15). Harris et al. describe labeling the cell nucleus with a label being a fluorophore specific for DNA (col. 27, lines 16-20). Harris et al. describe determining the amount of a first and second fluorescently labeled species to determine the activity of a compound (col. 27, lines 28-34). Harris et al. describe the use of various binary masks, including one for cytoplasmic intensity in Figures 20A-D. Harris et al. describe determining fluorescent intensities (col. 27, lines 28-34), using a binary mask (col. 27, lines 56-58), searching the bitmap for objects (col. 27, lines 58-67), and continuing analysis on objects passing the filter criteria to calculate intensities of the objects associated with a particular mask (col. 28, lines 1-34). Harris et al. describe creating annular masks (col. 28, lines 15-34) which can reasonably be interpreted to form for objects such as the cell membrane. Harris et al. describe calculating the ratio of eroded annular intensities for each object and determining average intensities as well as comparing ratio fractions for the fluorescently-labeled species (col. 26, lines 46-51). Harris et al. describe creating two daughter masks, one being an annular

extension of a primary mask and one being an eroded version of the primary mask for a cell (col. 28, lines 38-47) which is reasonably interpreted to include a cell membrane mask and a cytoplasmic mask. Harris et al. describe creating ratios of the quantities on a cell-by-cell basis (col. 28, lines 44-47). Harris et al. describe determining the location and intensities of the multiple fluorescently labeled species as well as their correlations (col. 7, lines 11-19). Harris et al. describe performing the imaging at a single or multiple time points (col. 7, lines 19-27). Harris et al. describe acquiring data on individual cells to constitute data for a cell population (col. 9, lines 20-25). Harris et al. describe using fluorescently labeled antibodies (col. 20, line 29 and col. 27, lines 23-27). Harris et al. describe using membranes from cells in a receptor-binding assay using fluorescent labels (col. 20, line 48 to col. 21, line 49). Harris et al. describe comparing images from wells containing a test compound to control wells (col. 21, lines 50-56). Harris et al. describe a fluorescence signal of interest might originate from the receptor in the nucleus (col. 23, lines 26-29) which is a form of identification as stated in claim 44. Harris et al. describe identifying an object to which fluorescently labeled species bind (col. 25, lines 43-56 and col. 26, lines 52-61).

Although Harris et al. describe the above-mentioned method computing device, they do not describe having this program on a machine readable storage medium using computer-executable instructions. *In re Venner* 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) states that it is obvious to computerize a manual activity. The court held that broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over prior art as stated in MPEP § 2144.04, Part III.

A person of ordinary skill in the art would have been motivated to enhance the procedures of detecting distribution of cellular components, as stated by Harris et al., by including these steps on a computer readable medium in order to quickly screen a large number of compounds, as stated by Harris et al. (col. 1, lines 44-45). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to place method and apparatus instructions including data processing routines (Harris et al., col. 1, lines 15-22) on a machine readable storage medium for a manual activity (as discussed by *In re Venner*) such as basic identification of cellular component distribution in cells (as stated by Harris et al), because this information would enhance and quicken access to the identification of compounds to be used as pharmaceutical agents, as stated by Harris et al. (col. 1, lines 15-22 and 44-45 and col. 2, lines 53-65).

Thus, Harris et al., in view of *In re Venner*, motivate the instant invention.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (703) 308-6043. The examiner can normally be reached Monday through Friday from 8 A.M. to 4:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

September 16, 2003

ARDIN H. MARSCHEL
PRIMARY EXAMINER